Published in final edited form as:

Clin Neuropsychol. 2012 October ; 26(7): 1201–1216. doi:10.1080/13854046.2012.728626.

Yes/No Versus Forced-Choice Recognition Memory in Mild Cognitive Impairment and Alzheimer's Disease: Patterns of Impairment and Associations with Dementia Severity

Lindsay R. Clark¹, Nikki H. Stricker^{2,3}, David J. Libon⁴, Lisa Delano-Wood^{5,6}, David P. Salmon⁷, Dean C. Delis^{5,6}, and Mark W. Bondi^{5,6}

¹San Diego State University/University of California San Diego Joint Doctoral Program in Clinical Psychology, San Diego, CA, USA

²Veterans Affairs Boston Healthcare System, Boston, MA, USA

³Department of Psychiatry, Boston University School of Medicine, Boston, MA, USA

⁴Department of Neurology, Drexel University, College of Medicine, Philadelphia, PA, USA

⁵Department of Psychiatry, UC San Diego, School of Medicine, La Jolla, CA, USA

⁶Department of Veterans Affairs, San Diego Healthcare System, San Diego, CA, USA

⁷Department of Neurosciences, UC San Diego, School of Medicine, La Jolla, CA, USA

Abstract

Memory tests are sensitive to early identification of Alzheimer's disease (AD) but less useful as the disease advances. However, assessing particular types of recognition memory may better characterize dementia severity in later stages of AD. We sought to examine patterns of recognition memory deficits in individuals with AD and mild cognitive impairment (MCI). Memory performance and global cognition data were collected from participants with AD ($n=37$), MCI ($n=37$), and cognitively intact older adults (normal controls, NC; $n=35$). One-way analyses of variance (ANOVAs) examined differences between groups on yes/no and forced-choice recognition measures. Individuals with amnesic MCI performed worse than NC and nonamnesic MCI participants on yes/no recognition, but were comparable on forced-choice recognition. AD patients were more impaired across yes/no and forced-choice recognition tasks. Individuals with mild AD (>120 Dementia Rating Scale, DRS) performed better than those with moderate-to-severe AD (<120 DRS) on forced-choice recognition, but were equally impaired on yes/no recognition. There were differences in the relationships between learning, recall, and recognition performance across groups. Although yes/no recognition testing may be sensitive to MCI, forced-choice procedures may provide utility in assessing severity of anterograde amnesia in later stages of AD. Implications for assessment of insufficient effort and malingering are also discussed.

Keywords

Recognition memory; Alzheimer's disease; Mild cognitive impairment; Dementia severity; Neuropsychology

INTRODUCTION

Alzheimer's disease (AD) is typically characterized by initial deficits in episodic memory followed by subsequent decline in additional cognitive domains (Salmon & Bondi, 2009). The episodic memory deficit is usually portrayed by poor performance on recall and recognition measures indicative of impairment in encoding and storing information. Although recognition memory is often perceived as either spared or impaired following brain dysfunction, it can be assessed using a variety of procedures (e.g., yes/no, multiple choice, forced choice) yielding significantly different results (Bennett, Golob, Parker, & Starr, 2006; Karlsson, Johansson, Adolfsson, Nilsson, & Dubuc, 2003; Westerberg et al., 2006). Importantly, various methods of assessing episodic memory dysfunction may be sensitive to different underlying cognitive constructs and neuropathological processes (Jernigan, Ostergaard, & Fennema-Notestine, 2001). For instance, delayed recall of list-learning measures has demonstrated exclusive correlations with hippocampal volume in AD, whereas recognition performance is more strongly associated with damage to perirhinal/entorhinal cortices (Wolk & Dickerson, 2011), subcortical white matter alterations (Price et al., 2009), and the integrity of regions with reciprocal connections to the hippocampus (Butler et al., 2012).

Although episodic memory decline is one of the earliest demonstrated cognitive impairments in AD, the nature of recognition memory deficits in individuals at greater risk of developing AD—that is, patients with mild cognitive impairment (MCI)—remains uncertain. Individuals with amnesic MCI tend to exhibit similar patterns of cognitive performance to those of healthy older adults on several measures, but often show an analogous pattern of memory and confrontation naming deficits when compared to their AD counterparts, such as profiles on verbal serial list learning tests that are similar, though less impaired, to profiles of those with AD (Delis, Kramer, Kaplan, & Ober, 2000; Greenaway et al., 2006; Libon et al., 2011; Ribeiro, Guerreiro, & De Mendonca, 2007). While some studies have reported globally impaired recognition memory in amnesic MCI (Bennett et al., 2006; Wolk, Signoff, & DeKosky, 2008), others have found impaired yes/no, but intact forced-choice performance (Westerberg et al., 2006). Yes/no recognition involves the individual presentation of previously studied words and distractor words and requests the patient to respond “yes” or “no” based on whether the word was on the study list. Forced-choice recognition involves the presentation of a pair of words (one target and one distractor) and requests the patient to choose which word was on the study list. Improving the specificity and reliability of the MCI diagnosis by assessing multiple cognitive domains, requiring at least two impaired scores for the diagnosis of MCI, and examining patterns of performance in both amnesic and nonamnesic subtypes, may improve understanding of recognition deficits in individuals at risk for dementia and provide information about potential differences between subtypes in underlying etiology.

While memory performance is sensitive to the early detection of AD (see Salmon & Bondi, 2009, for review), such testing has not proven helpful for determining the severity of the amnesia as the illness progresses due to early and severe deficits on these memory tasks (Locascio, Growdon, & Corkin, 1995). However, studies have demonstrated that individuals are capable of recognizing substantial levels of information when forced-choice procedures are employed (Christensen, Kopelman, Stanhope, Lorentz, & Owen, 1998; Karlsson et al., 2003). Furthermore, in our clinical practice we have noted that individuals with mild AD tend to perform well on the forced-choice condition of the California Verbal Learning Test—Second Edition (CVLT–II), whereas patients with moderate-to-severe AD often do not. Although forced-choice testing is typically used to assess inadequate effort or malingering given that even moderately to severely brain-damaged populations obtain relatively high accuracy scores, its potential as a clinical tool for assessing genuine memory impairment has

generally not been examined. However, forced-choice testing may have the potential to provide a means for assessing amnesia severity in individuals diagnosed with AD.

The current study assessed recognition memory performance using both yes/no and forced-choice procedures to examine the effect of test format on performance in individuals with AD, amnesic and nonamnesic MCI, and cognitively intact older adults. The major aims of the study were to: (a) investigate the influence of dementia severity in AD on recognition memory, particularly in regards to yes/no versus forced-choice formats; and (b) examine the nature of recognition impairments in amnesic and nonamnesic MCI subtypes across yes/no and forced-choice testing formats. As has been demonstrated in past studies, we expected healthy older adults and individuals with MCI to outperform individuals with AD on both recognition memory procedures. We hypothesized that individuals with MCI would perform worse than cognitively normal older adults on yes/no but not forced-choice recognition procedures and that the amnesic MCI subgroup would score lower than the nonamnesic MCI subgroup on yes/no recognition. Lastly, we hypothesized that dementia severity would show a differential relationship with the two recognition memory formats in the AD group. Given previous findings showing that AD patients often exhibit deficits on explicit memory procedures (e.g., recall; yes/no recognition) that are disproportionate to other areas of cognition in early stages of the disease, we predicted that forced-choice recognition memory but not yes/no recognition memory performance would be significantly related to dementia severity in AD.

METHOD

Participants

Data from 109 older adults were extracted from a larger battery of neuropsychological tests administered at the University of California San Diego Alzheimer's Disease Research Center (ADRC) or the Veterans Affairs San Diego Healthcare System (VASDHS). Specifically, data from 27 individuals with AD were collected at the ADRC, and data from all remaining participants (35 cognitively normal older adults, 37 individuals with MCI, and 10 individuals with AD) were collected at the VASDHS. Participants at both settings were administered a standardized battery of tests by trained research assistants or psychometrists. The tests given were comparable and lasted similar lengths of time (approximately 3–4 hours) across settings, but tests were administered in a different order across the two settings. This study was approved by the institutional review boards at UCSD and the VA San Diego Healthcare System.

Thirty-seven individuals were diagnosed with probable Alzheimer's disease (AD) based on the criteria established by the National Institute of Neurological and Communicative Disorders and Stroke–Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) workgroup (McKhann et al., 1984). Thirty-seven individuals were diagnosed with mild cognitive impairment (MCI) according to criteria set forth by Jak et al. (2009) by the presence of at least two test scores within a cognitive domain that fell one standard deviation below normative means. At least three measures from each of five cognitive domains (memory, attention, language, visuospatial functioning, and executive functioning) were administered and used in the classification of MCI (see Jak et al., 2009, for specific measures). Notably, recognition memory scores were not used in the diagnosis of MCI. The final sample included 18 amnesic (7 single-domain, 11 multidomain) and 19 nonamnesic MCI (13 single-domain, 6 multidomain) participants. The single-domain nonamnesic group included participants who exhibited primarily dysexecutive, visuospatial, or language impairments, and the multidomain nonamnesic participants all displayed dysexecutive symptoms in addition to a visuospatial or attention impairment. Thirty-five individuals classified as cognitively normal were matched to the AD and MCI groups on age, gender,

and education. As displayed in Table 1, there were no significant differences between the AD, MCI, and normal control (NC) groups on age, $F(2, 105)=0.98$, $p=.38$, gender, $\chi^2(2, N=109)=2.04$, $p=.36$, or education, $F(2, 105)=2.42$, $p=.09$.

Materials and procedure

Data from the California Verbal Learning Test II (CVLT–II; Delis et al., 2000) and the Dementia Rating Scale (DRS; Mattis, 1988) were extracted from a larger battery of neuropsychological tests administered for research or clinical purposes. The CVLT–II measures recall and recognition of two word lists over several immediate and delayed memory trials and was administered according to standardized instructions. Each list is composed of 16 words: 4 words from each of four semantic categories. In the first five trials, examinees were asked to recall words from List A immediately after list presentation. The second list (List B) was presented for one trial immediately following the fifth trial of List A and served as an interference list. This was followed by short-delay free recall and cued recall trials of List A. Following a 20-minute delay, long-delay free recall, long-delay cued recall, and yes/no recognition trials of List A were administered.

The yes/no recognition trial consisted of the 16 target words and 32 distractor words. Correct “yes” responses were recorded as hits, and incorrect “yes” responses were recorded as false positives. A recognition discriminability measure (d') that was independent of response bias was calculated and was used as the primary outcome variable for yes/no recognition performance. Ten minutes after completion of the yes/no recognition trial, participants were given the optional forced-choice recognition testing for List A. The examinee was read 16 pairs of words and was asked to identify the word from each pair that was from List A. Half of the nontarget words were concrete (FC-concrete), and half were abstract (FC-abstract). The forced-choice recognition trial was, by design, intended to yield a ceiling effect to assist in the assessment of test-taking effort.

Critical items are items that should have been correctly endorsed on the forced-choice recognition trial based on earlier performance and are included on the CVLT–II to assist in detecting suboptimal effort. The two critical items are (a) target words recalled at least once on immediate- or delayed-recall trials but missed on forced-choice recognition (CI-recall), and (b) target words that were hits on yes/no recognition but missed on forced-choice recognition (CI-recognition). In the normative sample, the occurrence of these types of errors was extremely rare, even in the oldest subjects.

The Dementia Rating Scale is a widely used standardized, 144-point test of global cognition assessing attention (37 points), initiation/perseveration (37 points), conceptualization (39 points), construction (6 points), and memory (25 points). This measure has proven to be reliable and valid in characterizations of dementia (see Monsch et al., 1995) and was used to assess dementia severity.

Statistical analyses

One-way analysis of variance (ANOVA) was used to examine group differences on all continuous measures except forced-choice and critical items. Nonparametric Kruskal–Wallis tests were used with the latter items due to their skewed distributions. Post hoc pairwise comparisons for all continuous measures except forced-choice and critical items were conducted using Tukey protection for multiple pairwise comparisons. Post hoc comparisons for these latter items were conducted using Mann–Whitney U tests. The effect of dementia severity (DRS total score) on forced-choice and yes–no recognition performance within the AD group was examined by comparing individuals with mild AD (defined as $DRS \geq 120$) or moderate-to-severe AD (defined as $DRS < 120$). Spearman correlations were computed to

examine the relationship between performance on recognition memory conditions and immediate and delayed recall performance.

RESULTS

Yes/no recognition memory performance across groups

Table 1 summarizes demographic characteristics and CVLT–II performance across groups. One-way ANOVAs revealed significant group differences on yes/no recognition discriminability, $F(3, 105)=61.82$; $p<.001$, $\eta_p^2=.64$, total recognition hits, $F(3, 105)=11.73$, $p<.001$, $\eta_p^2=.25$, and total false-positive errors, $F(3, 105)=37.74$, $p<.001$, $\eta_p^2=.52$. Post hoc analyses revealed that individuals with AD had significantly lower yes/no recognition discriminability scores than the NC group ($p<.001$) and both MCI subtypes ($p<.001$). Additionally, the amnesic MCI subgroup had significantly lower yes/no recognition discriminability scores than the nonamnesic subgroup ($p=.01$). Furthermore, the amnesic MCI subgroup displayed lower yes/no recognition discriminability than NC participants ($p<.001$), whereas the nonamnesic subgroup did not ($p=.30$).

Further examination of yes/no recognition performance indicated that participants with AD had significantly fewer recognition hits than the NC group ($p<.001$) and greater false-positive errors than both NC ($p<.001$) and MCI ($p<.001$) groups. Although amnesic and nonamnesic MCI subgroups achieved similar numbers of recognition hits in comparison to the NC group ($ps>.05$), the lower total recognition discriminability score in amnesic MCI was driven by a greater number of false-positive errors ($p<.01$) than the NC group. Both MCI subgroups demonstrated a similar ability to discriminate between target list words and novel distractor words compared to the cognitively intact group (CVLT novel recognition discriminability; $ps>.08$). However, the amnesic MCI group performed significantly worse than nonamnesic and NC groups at discriminating target words from distractor words that had been presented during the List B interference condition (CVLT source recognition discriminability; $ps<.05$) or that were semantically related to the target words (CVLT semantic recognition discriminability; $ps<.05$).

Forced-choice recognition memory performance across groups

Significant group differences were evident on the forced-choice recognition memory condition. Specifically, the four groups differed on total percentage correct, $\chi^2(3, N=109)=48.30$, $p<.001$; percentage concrete words correct, $\chi^2(3, N=109)=23.83$, $p<.001$; percentage abstract words correct, $\chi^2(3, N=109)=43.44$, $p<.001$; CI-recall, $\chi^2(3, N=109)=27.46$, $p<.001$; and CI-recognition, $\chi^2(3, N=109)=31.72$, $p<.001$. Post hoc analyses were conducted using an adjusted alpha level ($\alpha=.0125$) to protect against Type I errors. AD participants demonstrated worse overall accuracy on the forced-choice measure than did the NC ($p<.001$), amnesic MCI ($p<.001$), and nonamnesic MCI ($p<.001$) participants. The AD group was less accurate on both concrete and abstract words than the NC ($ps<.001$), amnesic MCI ($ps<.01$), and nonamnesic ($ps<.0125$) groups. In contrast, the MCI group (amnesic and nonamnesic) and the NC group performed similarly on overall forced-choice recognition ($p=.09$) and additional forced-choice variables (all p -values $>.03$). Lastly, forced-choice recognition performance was not associated with yes/no recognition performance in the NC group ($r_s=-.01$, $p=.97$) or the amnesic MCI ($r_s=.10$, $p=.69$) or nonamnesic MCI ($r_s=.12$, $p=.63$) subgroups, but neared significance in the AD group ($r_s=.30$, $p=.07$).

Relationship between recall and recognition memory performance across the sample

Spearman correlations examined the relationship between yes/no and forced-choice recognition memory and performance on immediate and delayed recall conditions of the

CVLT-II. Within the AD group, immediate recall (List A Trials 1–5 total recall) was significantly associated with FC-total correct ($r_s=.43$, $p<.01$), but not with total yes/no recognition discriminability ($p=.51$). The number of words recalled on the long-delay free recall condition was related to both FC-total correct ($r_s=.49$, $p<.01$) and total yes/no recognition discriminability ($r_s=.34$, $p=.04$). Furthermore, within the AD group there was a significant correlation between dementia severity (DRS total score) and forced-choice performance ($r_s=.41$; $p=.01$), but no association between dementia severity and yes/no recognition performance ($p=.76$).

Conversely, immediate recall (List A Trials 1–5 total recall) was not significantly related to FC-total in the MCI ($p=.83$) or NC ($p=.75$) groups, but was associated with total yes/no recognition discriminability in the MCI ($r_s=.72$, $p<.001$) and NC ($r_s=.43$; $p<.01$) groups. Long-delay free recall performance was not related to FC-total in MCI ($p=.57$) or NC ($p=.89$) participants, but did relate to performance on yes/no recognition discriminability in both of these groups ($r_s=.71$, $p<.001$). There were no significant correlations between DRS total score and recognition performance in the NC or MCI groups. See Table 2 for a complete list of correlations.

Relationship between recognition memory and dementia severity in AD

The relationship between dementia severity and AD was examined further by subdividing this group on the basis of their DRS total score into mild (≥ 120 DRS; $N=16$) and moderate-to-severe (<120 DRS; $N=21$) subgroups (see Table 3). The two subgroups showed comparable performances on overall yes/no recognition memory ($p=.29$). However, the mild AD group performed better than the moderate-to-severe group on forced-choice recognition memory ($p<.01$). Specifically, these differences were driven by worse performance in the moderate-to-severe subgroup on concrete forced-choice items ($p<.05$). The groups performed similarly on the abstract forced-choice items ($p=.07$). In addition, the moderate-to-severe AD group demonstrated a higher rate of CI-recognition errors than the mild AD group ($p<.05$), and they demonstrated a trend towards an increased rate of CI-recall errors ($p=.05$). Figure 1 provides a summary of yes/no and forced-choice performances across all study groups.

DISCUSSION

The aim of the current study was to examine patterns of recognition memory using different testing formats, with particular interest in understanding these patterns in individuals at risk for dementia and in those at different stages of Alzheimer's disease. This aim was investigated by comparing patterns of recognition memory performance on the yes/no and forced-choice recognition conditions of the California Verbal Learning Test-II in individuals with AD, MCI, and cognitively intact older adults. Our findings indicate a degeneration of recognition memory abilities from normal aging through moderate–severe stages of dementia, in which normal older adults demonstrated equally high recognition memory performance on both test formats, individuals with amnesic MCI performed similarly to normal controls on the forced-choice task but worse on the yes/no recognition task, and individuals with AD performed worse on both recognition memory procedures than did normal control and MCI groups.

Our results showed that dementia severity was not associated with yes/no recognition performance, but was significantly associated with forced-choice recognition within the AD group. Specifically, both mild and moderate-to-severe AD subgroups had similar deficits on yes/no recognition testing, but the mild AD group performed significantly better than the moderate-to-severe AD group on the forced-choice recognition condition. These results suggest that while recall and yes/no recognition memory tasks may be good early indicators

of dementia, forced-choice recognition memory tasks may be clinically useful in characterizing dementia stages and the severity of amnesia in those with AD. Specifically, both AD subgroups performed well on forced-choice items that compared target words to abstract word foils, but the mild AD group performed significantly better on forced-choice items that compared target words to concrete word foils. This finding indicates that even moderately to severely demented individuals can perform reasonably well on forced-choice tasks that compare target words to distinct distractor words, but are less able to distinguish target words from similar distractor words. Additionally, the moderate-to-severe AD group committed more errors than the mild group on critical items, or items that should have been accurately endorsed based on earlier performance (e.g., words that were endorsed during recall or yes/no recognition conditions). Across the AD subgroups, recalling more words on the immediate recall trials was associated with greater accuracy on forced-choice testing, but not with better yes/no recognition performance. On the other hand, recalling more words on the delayed-recall trial was correlated with better performance on both yes/no and forced-choice tasks. The moderate-to-severe AD subgroup was significantly older than the mild AD subgroup, and therefore it is possible that the results could be due to an age effect. To ensure that age differences could not fully explain these findings, the data were reanalyzed including age as a covariate and again after matching the two subgroups by age, and the findings remained consistent with those reported above. Further, partial correlations between DRS severity and forced-choice performance controlling for age within the AD group retained significance for forced-choice total performance and forced-choice items that compared target words to concrete word foils ($p < .05$).

A dual-process model of recognition memory (Mandler, 1980; Yonelinas, 2002) provides an interesting framework for understanding the observed improved memory capacity in mild AD patients under forced-choice recognition procedures despite their severe levels of impairment on other measures of episodic memory. According to this model, two memory processes, recollection and familiarity, contribute to recognition memory performance. The relative sparing of forced-choice recognition memory performance in our mild AD participants is consistent with results suggesting that familiarity alone may support intact performance under a forced-choice recognition format. That is, AD patients may benefit from the relative familiarity of the targets versus distractors in making their responses (Dalla Barba, 1997). In contrast, yes/no recognition memory performance may be more dependent upon intact recollection (Westerberg et al., 2006). Consistent with this possibility, normal forced-choice recognition has been reported in the face of severe impairments in yes/no recognition in a patient with focal hippocampal damage (Holdstock et al., 2002), and intact familiarity processes have been found in other studies of early AD (Dalla Barba, 1997; Lekeu et al., 2003; Rauchs et al., 2007).

It has been proposed that recollection depends on the integrity of the hippocampus, whereas familiarity is associated with the integrity of other medial temporal lobe (MTL; e.g., perirhinal/entorhinal cortex) and neocortical regions (Brown & Aggleton, 2001). In addition, partial damage to structures within this region may still permit intact familiarity-based recognition, even when recollection-based recognition (e.g., yes/no) is impaired (Brown & Aggleton, 2001; Brown & Xiang, 1998; Westerberg et al., 2006). Though speculative, in mild AD the burden of neurofibrillary tangles in medial temporal regions may lie below a critical threshold that is necessary for impaired familiarity-based recognition performance, whereas the tangle burden in moderate-to-severe AD patients may have surpassed this threshold, resulting in impaired forced-choice recognition memory performance. Familiarity-based recognition performance may be expected to decline as AD pathology spreads to cortical association areas in the temporal, parietal, and frontal cortices (Braak & Braak, 1996). However, it has also been argued that yes/no and forced-choice testing procedures often differ on length and difficulty and that performance on both formats have

been shown to be equally impaired in individuals with hippocampal damage when the two tests are of similar length (Bayley, Wixted, Hopkins, & Squire, 2008). Furthermore, these researchers suggest that the hippocampus is involved in both types of recognition memory procedures and that the distinction between recollection/familiarity is unlikely related to the functional organization of the MTL (Wixted & Squire, 2010).

The majority of studies attempting to disentangle deficits in recollection and familiarity in MCI have found recollection, but not familiarity, to be impaired in amnesic MCI (Anderson et al., 2008; Serra et al., 2010; Westerberg et al., 2006), suggesting that a selective impairment in recollection is one of the earliest consequences of AD pathology. However, this finding is not universal. Some studies have reported reductions in both recollection and familiarity processes, arguing that both processes equally impact early recognition memory decline (Algarabel et al., 2009; Wolk et al., 2008). Our findings indicated that, in contrast to individuals with AD, those with MCI perform significantly worse than normal controls on the yes/no recognition test but normally on the forced-choice task. This result was particularly driven by the amnesic rather than the nonamnesic MCI subtype. Interestingly, the decreased recognition memory performance in the amnesic MCI group was driven by an increase in false-positive errors, rather than a reduced number of correct responses. This pattern is similar to previous findings in this population (Greenaway et al., 2006; Libon et al., 2011). Furthermore, our results indicated that, while both MCI subtypes were comparable at discriminating target words from novel distractor words, our amnesic subgroup was worse at discriminating target words from semantically related distractor words and from distractor words that were presented on the interference list (e.g., List B). The latter finding is consistent with studies demonstrating that individuals with amnesic MCI are more sensitive to proactive interference than normal older adults (Hanseeuw, Seron, & Ivanoiu, 2010; Loewenstein, Acevedo, Agron, & Duara, 2007).

Since amnesic MCI is more obviously associated with memory impairment, few studies have examined patterns of recognition performance in nonamnesic MCI. Nevertheless, at least one study has demonstrated that both subtypes are equally likely to exhibit AD-related pathology at autopsy (Schneider, Arvanitakis, Leurgans, & Bennett, 2009), suggesting that current definitions of MCI subtypes may not sufficiently capture underlying etiologic differences. Additionally, a recent autopsy study reported that approximately 25% of individuals with AD develop disease-related pathology in an atypical pattern, including some that spare hippocampal regions (Murray et al., 2011), and therefore it is possible that nonamnesic presentations of cognitive impairment may represent variations in AD pathology development and/or the presence of other pathology, such as cerebro-vascular disease, that may progress to a non-AD dementia syndrome (e.g., vascular dementia). Consistent with our findings, Libon and colleagues (2011) also observed that individuals with nonamnesic MCI did not differ from normal controls in recognition memory performance. Unlike our findings, their nonamnesic MCI group also endorsed more foils that had been presented on the interference word list. Although more research is warranted, evidence suggests that different patterns of recognition memory performance can be helpful in distinguishing subtypes of MCI. Furthermore, these variations in performance patterns may inform potential etiological differences among MCI subtypes.

Lastly, we examined the relationship between recognition memory and performance on immediate and delayed recall conditions. Our results showed that in normal controls and individuals with MCI, immediate and delayed recall performances were related to recognition memory performance as assessed by either yes/no or forced-choice testing procedures. In contrast, immediate recall performance in the AD group was related to forced-choice total correct, but not to total yes/no recognition discriminability. Delayed recall was related to performance on both recognition testing formats in the AD group. This

distinction may relate to suggestions that both yes/no recognition and delayed recall are strongly associated with hippocampal function, whereas forced-choice testing and immediate recall may rely on additional non-MTL cortical regions (Westerberg et al., 2006; Wolk & Dickerson, 2011). In this case, immediate recall performance may be more reflective of working memory ability (e.g., echoing back the last words heard) whereas forced-choice performance may reflect a general familiarity of the word but a loss of any of the contextual details needed to perform accurately on a delayed-recall or yes/no recognition task.

Regardless of the underlying neural mechanisms, our observations of dissociations between yes/no and forced-choice measures in amnesic MCI and AD have important scientific and clinical implications. First, individuals with amnesic MCI exhibited significantly more false-positive errors on yes/no recognition testing than did normally aging older adults, which may assist in identifying older adults at higher risk of developing AD. Second, relatively preserved forced-choice recognition memory in mild AD patients reflects some capacity to learn and retain at least partial memory traces. Lastly, forced-choice testing may provide a valuable clinical means for *gauging* the severity of amnesia associated with AD. This finding is important because most currently available memory procedures cannot measure the severity of memory impairment in patients with AD due to prominent floor effects in the moderate-to-severe dementia stages. The capacity for forced-choice recognition measures to assist clinicians in determining the level of dementia severity in more advanced stages of AD may allow them to make more accurate prognosis and customized care recommendations to patients and their caregivers.

Our findings may also have clinical implications for detecting suboptimal effort on neuropsychological tests. Previous studies have shown that even moderately to severely impaired patients are able to perform at high levels (e.g., approximately 89% or more correct) on forced-choice recognition tasks (Green & Iverson, 2001). Similarly, our study indicates that (a) mild AD patients tend to achieve perfect or near-perfect (one error) scores on the forced-choice trial of the CVLT-II; and (b) even moderately to severely impaired individuals with AD perform, on average, above chance on the forced-choice task (81% accuracy). However, when examining specific items, it is clear that the moderate-severe AD subgroup demonstrated more errors on forced-choice items comparing target words with concrete word foils than with abstract word foils. Indeed, the moderately to severely impaired AD group performed almost perfectly on items that compared target words with abstract words as foils. This finding suggests that items that compare target words with abstract foils on the forced-choice task are likely to be most useful in detecting suboptimal effort.

Limitations of the current study should be taken into consideration. Although the sample size in this study is comparable to other studies in this area, it is relatively small, particularly when comparing mild and moderate AD subgroups. Future studies with larger mild and moderate AD groups will be necessary to validate these findings. Additionally, the forced-choice task had fewer items and was likely less difficult to complete than the yes/no recognition task. Because of this potential difference, it is difficult to clearly determine the differential impact of recollection or familiarity (versus an easy/difficult distinction) in this study and limits the current findings specifically to the CVLT. However, previous studies that had similarly difficult yes/no and forced-choice tasks (e.g., Westerberg et al., 2006) found a pattern of results similar to our own. Additional experimental studies investigating the relationship between familiarity and recollection-based recognition memory and dementia severity in AD are needed to validate these results and facilitate any conclusions about the neural correlates of these two aspects of recognition memory. Despite these limitations, our results indicate that recognition memory declines along a continuum from

normal aging to amnesic MCI to AD. Furthermore, yes/no recognition testing may be more sensitive than forced-choice testing in MCI or patients at risk for developing AD. However, forced-choice testing may be useful in gauging the severity of amnesia and dementia in individuals in later stages of AD.

Acknowledgments

This work was supported by Alzheimer's Association Grants IIRG 07-59343 (M.B.) and National Institute on Aging Grants R01 AG012674 (M.B.), K24 AG026431 (M.B.), and P50 AG05131 (D.S.). Dean Delis has a financial interest in one of the neuropsychological measures administered as part of this study. He is the lead author of the California Verbal Learning Test II, published by Pearson. There are no other financial or additional conflicts of interest pertaining to this manuscript. The authors gratefully acknowledge the assistance of Gali Weissberger, Jason Gravano, and Ashley McCauley for their assistance in data collection as well as the staff, patients, and volunteers of the University of California San Diego Alzheimer's Disease Research Center (UCSD ADRC).

REFERENCES

- Algarabel S, Escudero J, Mazon JF, Pitarque A, Fuentes M, Peset V, Lacruz L. Familiarity-based recognition in the young, healthy elderly, mild cognitive impaired, and Alzheimer's patients. *Neuropsychologia*. 2009; 47:2056–2064. [PubMed: 19467356]
- Anderson ND, Ebert PL, Jennings JM, Grady CL, Cabeza R, Graham SJ. Recollection- and familiarity-based memory in healthy aging and amnesic mild cognitive impairment. *Neuropsychology*. 2008; 22(2):177–187. [PubMed: 18331160]
- Bayley PJ, Wixted JT, Hopkins RO, Squire LR. Yes/no recognition, forced-choice recognition, and the human hippocampus. *Journal of Cognitive Neuroscience*. 2008; 20(3):505–512. [PubMed: 18004951]
- Bennett IJ, Golob EJ, Parker ES, Starr A. Memory evaluation in mild cognitive impairment using recall and recognition tests. *Journal of Clinical and Experimental Neuropsychology*. 2006; 28:1408–1422. [PubMed: 17050267]
- Braak H, Braak E. Evolution of the neuropathology of Alzheimer's disease. *Acta Neurologica Scandinavica*. Supplementum. 1996; 165:3–12.
- Brown MW, Aggleton JP. Recognition memory: What are the roles of the perirhinal cortex and hippocampus? *Nature Reviews: Neuroscience*. 2001; 2:51–61.
- Brown MW, Xiang JZ. Recognition memory: Neuronal substrates of the judgment of prior occurrence. *Progress in Neurobiology*. 1998; 55:149–189. [PubMed: 9618747]
- Butler T, Blackmon K, Zaborsky L, Wang XY, DuBois J, Carlson C, Thesen T. Volume of the human septal forebrain region is a predictor of source memory accuracy. *Journal of the International Neuropsychological Society*. 2012; 18:157–161. [PubMed: 22152217]
- Christensen H, Kopelman MD, Stanhope N, Lorentz L, Owen P. Rates of forgetting in Alzheimer dementia. *Neuropsychologia*. 1998; 36:547–557. [PubMed: 9705065]
- Dalla Barba G. Recognition memory and recollective experience in Alzheimer's disease. *Memory*. 1997; 5:657–672. [PubMed: 9497906]
- Delis, DC.; Kramer, JH.; Kaplan, E.; Ober, BA. California Verbal Learning Test: Second Edition. Psychological Corporation; San Antonio, TX: 2000.
- Green P, Iverson GL. Validation of the computerized assessment of response bias in litigating patients with head injuries. *The Clinical Neuropsychologist*. 2001; 15:492–497. [PubMed: 11935450]
- Greenaway MC, Lacritz LH, Binengar D, Weiner MF, Lipton A, Cullum CM. Patterns of verbal memory performance in mild cognitive impairment, Alzheimer's disease, and normal aging. *Cognitive and Behavioral Neurology*. 2006; 19:79–84. [PubMed: 16783130]
- Hanseeuw B, Seron X, Ivanoiu A. Increased sensitivity to proactive interference in amnesic mild cognitive impairment is independent of associative and semantic impairment. *Brain and Cognition*. 2010; 72:325–331. [PubMed: 19906479]
- Holdstock JS, Mayes AR, Roberts N, Cezayirli E, Isaac CL, O'Reilly RC, Norman KA. Under what conditions is recognition spared relative to recall after selective hippocampal damage in humans? *Hippocampus*. 2002; 12:341–351. [PubMed: 12099485]

- Jak AJ, Bondi MW, Delano-Wood L, Wierenga C, Corey-Bloom J, Salmon DP, Delis DC. Quantification of five neuropsychological approaches to defining mild cognitive impairment. *American Journal of Geriatric Psychiatry*. 2009; 17:368–375. [PubMed: 19390294]
- Jernigan TL, Ostergaard AL, Fennema-Notestine C. Mesial temporal, diencephalic, and striatal contributions to deficits in single word reading, word priming, and recognition memory. *Journal of the International Neuropsychological Society*. 2001; 7:63–78. [PubMed: 11253843]
- Karlsson T, Johansson I, Adolfsson R, Nilsson LG, Dubuc S. Recognition memory in Alzheimer's disease: A demonstration of a remarkable memory capacity in Alzheimer's disease. *Dementia and Geriatric Cognitive Disorders*. 2003; 15:6–9. [PubMed: 12457073]
- Lekeu F, Van Der Linden M, Degueldre C, Lemaire C, Luxen A, Franck G, Salmon E. Effects of Alzheimer's disease on the recognition of novel versus familiar words: Neuropsychological and clinico-metabolic data. *Neuropsychology*. 2003; 17:143–154. [PubMed: 12597083]
- Libon DJ, Bondi MW, Price CC, Lamar M, Eppig J, Wambach DM, Penney DL. Verbal serial list learning in mild cognitive impairment: A profile analysis of interference, forgetting, and errors. *Journal of the International Neuropsychological Society*. 2011; 17:905–914. [PubMed: 21880171]
- Locascio JJ, Growdon JH, Corkin S. Cognitive test performance in detecting, staging, and tracking Alzheimer's disease. *Archives of Neurology*. 1995; 52:1087–1099. [PubMed: 7487561]
- Loewenstein DA, Acevedo A, Agron J, Duara R. Vulnerability to proactive semantic interference and progression to dementia among older adults with mild cognitive impairment. *Dementia and Geriatric Cognitive Disorders*. 2007; 24:363–368. [PubMed: 17911981]
- Mandler G. Recognizing: The judgment of previous occurrence. *Psychological Review*. 1980; 87:252–271.
- Mattis, S. *Dementia Rating Scale: Professional manual*. Psychological Assessment Resources Inc; Odessa, FL: 1988.
- McKhann G, Drachman D, Folstein M, Katzman R, Price D, Stadlan EM. Clinical diagnosis of Alzheimer's disease: Report of the NINCDS-ADRDA work group under the auspices of the Department of Health and Human Services Task Force on Alzheimer's disease. *Neurology*. 1984; 34:939–944. [PubMed: 6610841]
- Monsch AU, Bondi MW, Salmon DP, Butters N, Thal LJ, Hansen LA, Klauber MR. Clinical validity of the Mattis Dementia Rating Scale in detecting dementia of the Alzheimer type: A double cross-validation and application to a community-dwelling sample. *Archives of Neurology*. 1995; 52:899–904. [PubMed: 7661728]
- Murray ME, Graff-Radford NR, Ross OA, Petersen RC, Duara R, Dickson DW. Neuropathologically defined subtypes of Alzheimer's disease with distinct clinical characteristics: A retrospective study. *Lancet Neurology*. 2011; 10:785–796. [PubMed: 21802369]
- Price CC, Garrett KD, Jefferson AL, Consentino S, Tanner JJ, Penney DL, Libon DJ. Leukoaraiosis severity and list-learning in dementia. *The Clinical Neuropsychologist*. 2009; 23:944–961. [PubMed: 19370451]
- Rauchs G, Piolino P, Mezenge F, Landeau B, Lalevee C, Pelerin A, Desgranges B. Autonoetic consciousness in Alzheimer's disease: Neuropsychological and PET findings using an episodic learning and recognition task. *Neurobiology of Aging*. 2007; 28:1410–1420. [PubMed: 16846667]
- Ribeiro F, Guerreiro M, De Mendonca A. Verbal learning and memory deficits in mild cognitive impairment. *Journal of Clinical & Experimental Neuropsychology*. 2007; 29:187–197. [PubMed: 17365254]
- Salmon DP, Bondi MW. Neuropsychological assessment of dementia. *Annual Review of Psychology*. 2009; 60:257–282.
- Schneider JA, Arvanitakis Z, Leurgans SE, Bennett DA. The neuropathology of probable Alzheimer disease and mild cognitive impairment. *Annals of Neurology*. 2009; 66:200–208. [PubMed: 19743450]
- Serra L, Bozzali M, Cercignani M, Perri R, Fadda L, Caltagirone C, Carlesimo GA. Recollection and familiarity in amnesic mild cognitive impairment. *Neuropsychology*. 2010; 24:316–326. [PubMed: 20438209]

- Westerberg CE, Paller KA, Weintraub S, Mesulam MM, Holdstock JS, Mayes AR, Reber PJ. When memory does not fail: Familiarity-based recognition in mild cognitive impairment and Alzheimer's disease. *Neuropsychology*. 2006; 20:193–205. [PubMed: 16594780]
- Wixted JT, Squire LR. The role of the human hippocampus in familiarity-based and recollection-based recognition memory. *Behavior and Brain Research*. 2010; 215:197–208.
- Wolk DA, Dickerson BC. Fractionating verbal episodic memory in Alzheimer's disease. *NeuroImage*. 2011; 54:1530–1539. [PubMed: 20832485]
- Wolk DA, Signoff ED, DeKosky ST. Recollection and familiarity in amnesic mild cognitive impairment: A global decline in recognition memory. *Neuropsychologia*. 2008; 46:1965–1978. [PubMed: 18328509]
- Yonelinas AP. The nature of recollection and familiarity: A review of 30 years of research. *Journal of Memory and Language*. 2002; 46:441–517.

Figure 1. California Verbal Learning Test–Second Edition (CVLT–II) yes/no and forced-choice recognition performance in mild Alzheimer’s disease (AD), moderate AD, amnesic mild cognitive impairment (aMCI), nonamnesic MCI (naMCI), and normal older adults.

Table 1

Demographic and neuropsychological characteristics of Alzheimer's disease, amnesic mild cognitive impairment, nonamnesic mild cognitive impairment, and normal control groups

Characteristic	AD (n = 37)	aMCI (n = 18)	naMCI (n = 19)	NC (n = 35)	Significance level <i>p</i>
Age (years) ^a	77.1 (8.4)	77.7 (8.2)	79.4 (8.0)	75.8 (8.8)	.51
Gender (F/M)	11/26	6/12	9/10	16/19	.42
Education (years) ^a	14.9 (2.7)	15.1 (2.6)	15.1 (2.8)	16.1 (1.9)	.19
DRS total score ^a	118.7 (8.2)	137.7 (3.5)	137.5 (3.5)	141.0 (3.0)	< .001
List A Trials 1-5 raw ^a	21.8 (8.5)	30.4 (5.2)	41.8 (9.3)	44.1 (7.0)	< .001
LD free recall raw ^a	0.9 (1.4)	4.7 (2.3)	9.1 (3.4)	9.5 (3.8)	< .001
Yes/no total recognition discriminability ^a	0.68 (0.6)	1.8 (0.7)	2.5 (1.0)	2.8 (0.7)	< .001
Recognition hits ^a	11.2 (2.9)	12.8 (2.5)	13.8 (1.8)	14.3 (1.6)	< .001
False-positive errors ^a	15.1 (7.1)	7.8 (4.8)	4.4 (4.5)	2.7 (2.9)	< .001
Yes/no source recognition discriminability ^a	0.7 (0.6)	1.8 (0.8)	2.4 (0.9)	2.8 (0.6)	< .001
Yes/no novel recognition discriminability ^a	0.6 (0.6)	1.7 (0.6)	2.3 (0.9)	2.7 (0.6)	< .001
Yes/no semantic recognition discriminability ^a	0.4 (0.6)	1.4 (0.6)	2.1 (1.0)	2.5 (0.7)	< .001
Forced-choice total accuracy (%) ^b	86.8 (14.4)	99.0 (2.3)	98.1 (4.0)	99.7 (1.4)	< .001
FC-concrete ^b	84.9 (20.8)	98.0 (4.6)	97.5 (5.0)	99.3 (2.8)	< .001
FC-abstract ^b	88.8 (13.8)	100.0 (0.0)	98.7 (3.8)	100.0 (0.0)	< .001
Critical item-recall ^b	1.0 (1.2)	0.2 (0.4)	0.3 (0.6)	0.03 (0.2)	< .001
Critical item-recog ^b	1.3 (1.9)	0.2 (0.4)	0.2 (0.4)	0.03 (0.2)	< .001

AD = Alzheimer's disease; aMCI = amnesic mild cognitive impairment; naMCI = nonamnesic mild cognitive impairment; NC = normal control; F = female; M = male; DRS = dementia rating scale; LD free recall = CVLT-II (California Verbal Learning Test-Second Edition) long-delay free recall; FC-concrete = CVLT-II forced-choice recognition accuracy on concrete items; CVLT-II FC-abstract = forced-choice recognition accuracy on abstract items; critical item-recall = CVLT-II target words recalled at least once on immediate or delayed recall but missed on forced-choice recognition; critical item-recog = CVLT-II target words that were hits on yes/no recognition but missed on forced-choice recognition.

^a *p*-values based on one-way analysis of variance (ANOVA);

^b *p*-values based on Kruskal-Wallis test.

Table 2

Spearman correlation matrices within Alzheimer's disease, mild cognitive impairment, and normal control groups

	Characteristic	CVLT-II List A 1-5 total	CVLT-II Long-delay free recall	CVLT-II Y/N recognition	CVLT-II FC-total
AD (n = 37)	DRS total score	.43**	.15	.05	.41*
	CVLT-II List A 1-5 total		.38*	.11	.43**
	CVLT-II long-delay free recall			.34*	.49**
	CVLT-II yes/no recognition discriminability				.30
	CVLT-II forced-choice (% accurate)				
Amnesic MCI (n= 18)	DRS total score	.14	.02	.15	.19
	CVLT-II List A 1-5 total		.32	.68**	-.23
	CVLT-II long-delay free recall			.55*	.28
	CVLT-II yes/no recognition discriminability				.10
	CVLT-II forced-choice (% accurate)				
Nonamnesic MCI (n= 19)	CVLT-II DRS total score	.39	.51*	.22	-.03
	CVLT-II List A 1-5 Total		.86***	.72***	.37
	CVLT-II long-delay free recall			.76***	.19
	CVLT-II yes/no recognition discriminability				.12
	CVLT-II forced-choice (% accurate)				
NC (n = 35)	DRS total score	.34*	.40*	.28	-.3
	CVLT-II List A 1-5 total		.52**	.43**	.06
	CVLT-II long-delay free recall			.72***	-.03
	CVLT-II yes/no recognition discriminability				-.01
	CVLT-II forced-choice (% accurate)				

AD = Alzheimer's disease; MCI = mild cognitive impairment; NC = normal controls; DRS = Dementia Rating Scale, CVLT-II = California Verbal Learning Test-Second Edition. Y/N = yes/no. FC = forced choice.

* $p < .05$.** $p < .01$.*** $p < .001$.

Table 3

Yes/no and forced-choice recognition memory performance in mild and moderate Alzheimer's disease

Characteristic	Mild AD (DRS $\geq$ 120) (N = 16)	Moderate AD (DRS < 120) (N = 21)	Significance level <i>p</i>
Age (years) ^a	71.9 (9.0)	81.1 (5.1)	.001
Gender (f/m)	5/11	6/15	.86
Education (years) ^a	14.4 (3.0)	15.2 (2.5)	.41
Yes/no recognition discriminability ^a	0.8 (0.5)	0.6 (0.6)	.29
Yes/no recognition hits ^a	11.4 (2.6)	11.1 (3.1)	.78
Yes/no false-positive errors ^a	14.1 (5.9)	15.8 (7.9)	.49
Forced-choice (% accurate) ^b	94.3 (6.2)	81.1 (16.3)	< .01
FC-concrete (% accurate) ^b	93.9 (12.8)	78.1 (23.3)	< .05
FC-abstract (% accurate) ^b	94.8 (6.1)	84.2 (16.2)	.07
Critical item-recall ^b	0.5 (0.8)	1.3 (1.3)	.05
Critical item-recognition ^b	0.4 (0.6)	2.0 (2.3)	< .05

AD = Alzheimer's disease; DRS = dementia rating scale; F = female; M = male; FC-concrete = forced-choice recognition accuracy on concrete items; FC-abstract = forced-choice recognition accuracy on abstract items; Critical item-recall = target words recalled at least once on immediate or delayed recall but missed on forced-choice recognition; Critical item-recognition = target words that were hits on yes/no recognition but missed on forced-choice recognition.

^a p-values based on *T-Test*.

^b p-values based on Mann-Whitney *U test*.